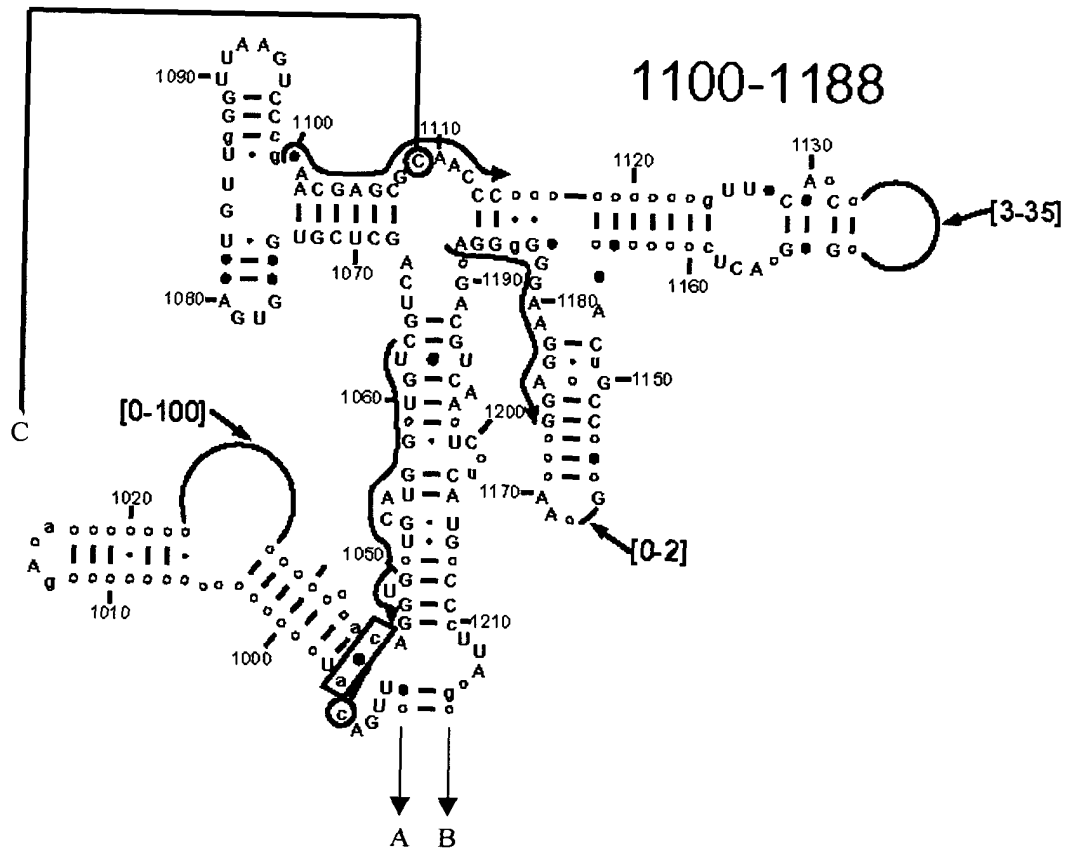


FIG. 1A-1



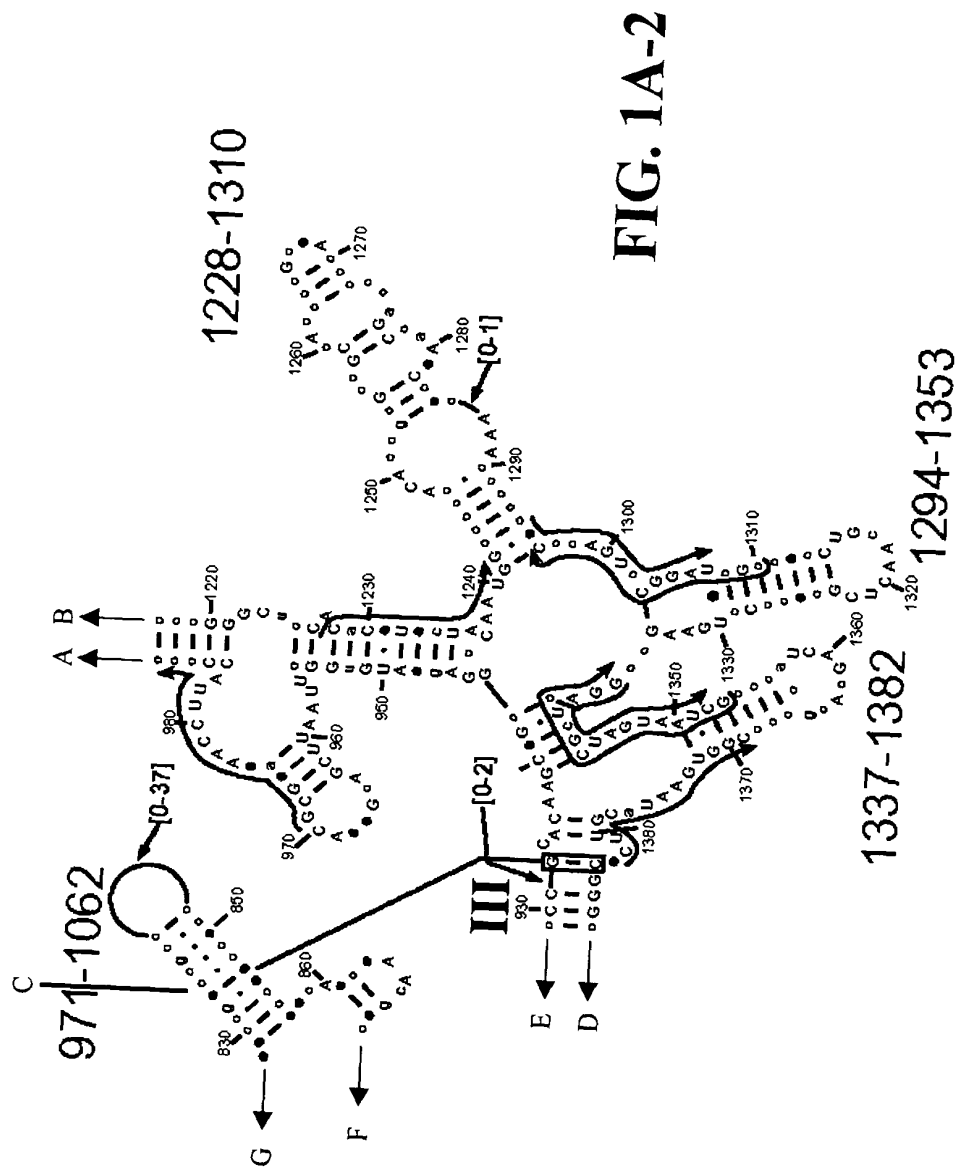


FIG. 1A-3

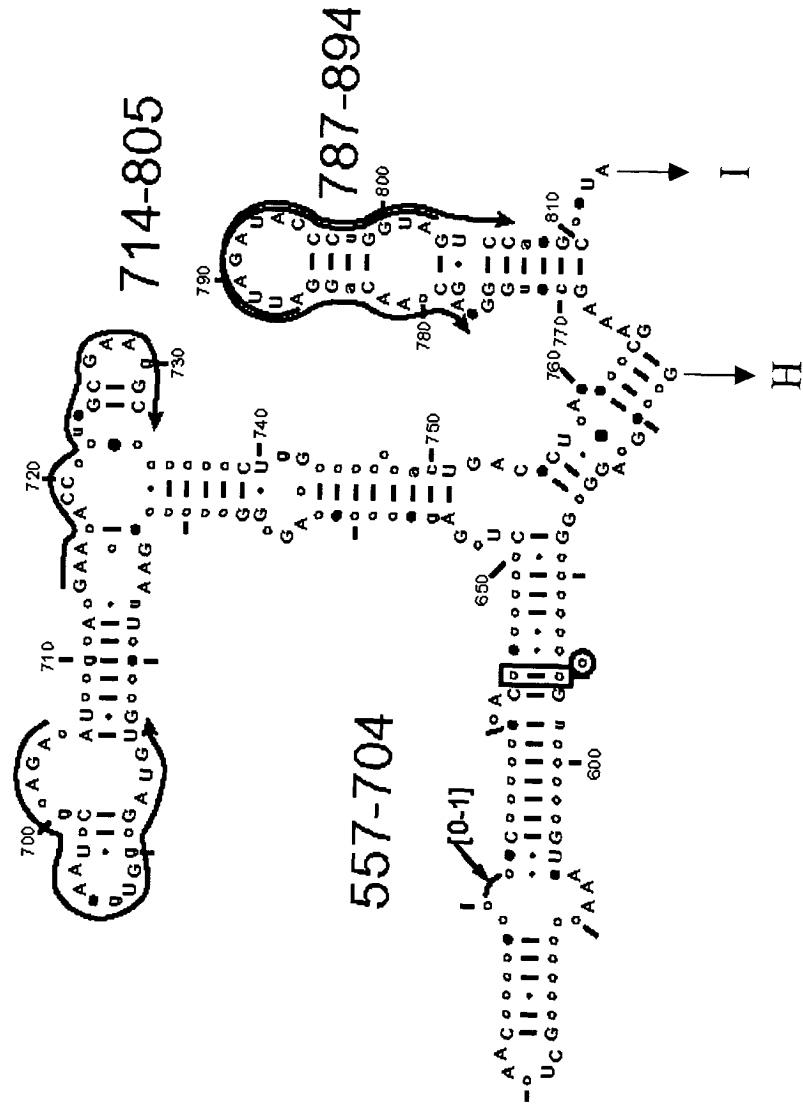


FIG. 1A-4

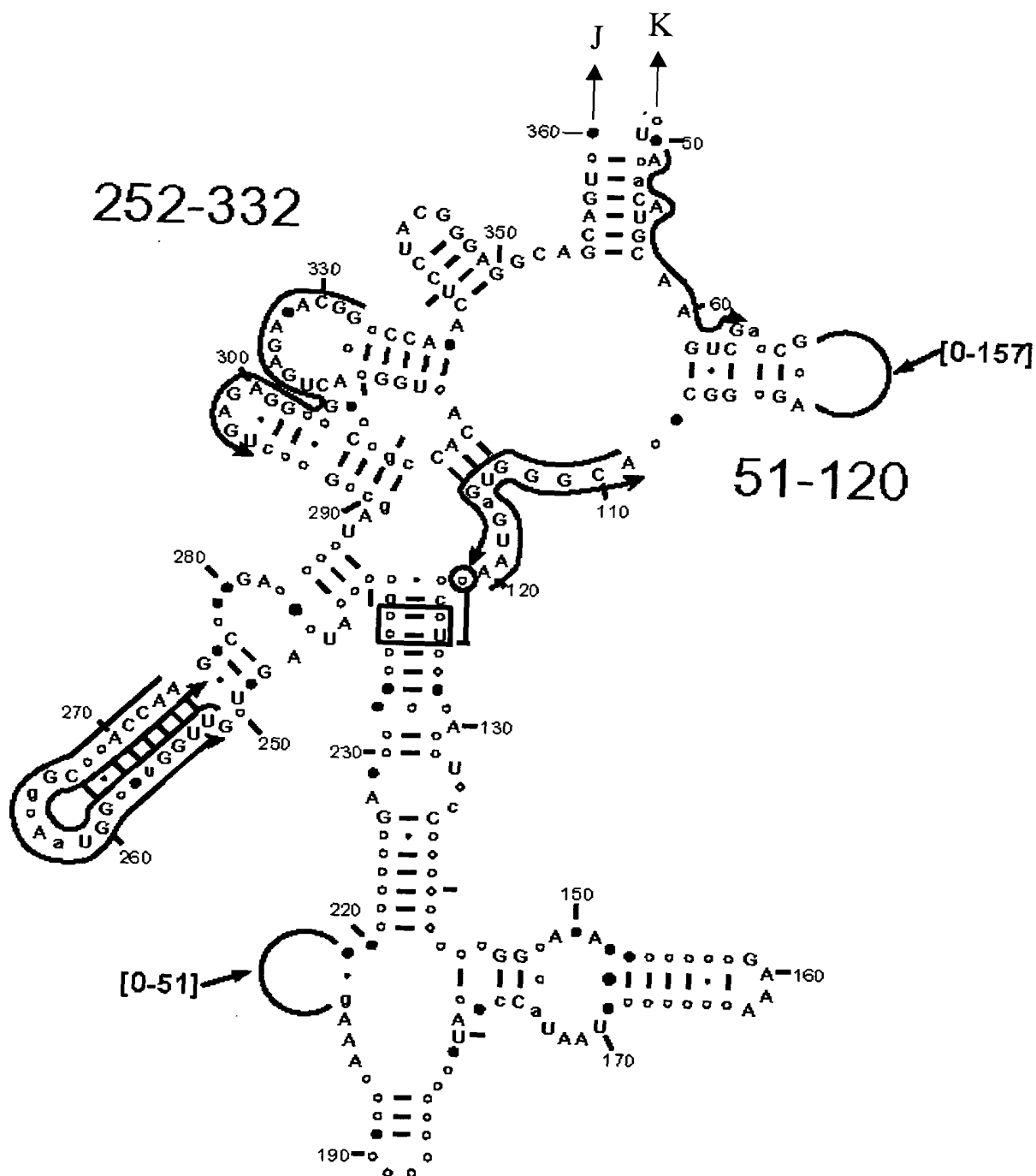


FIG. 1A-5

FIG. 1B

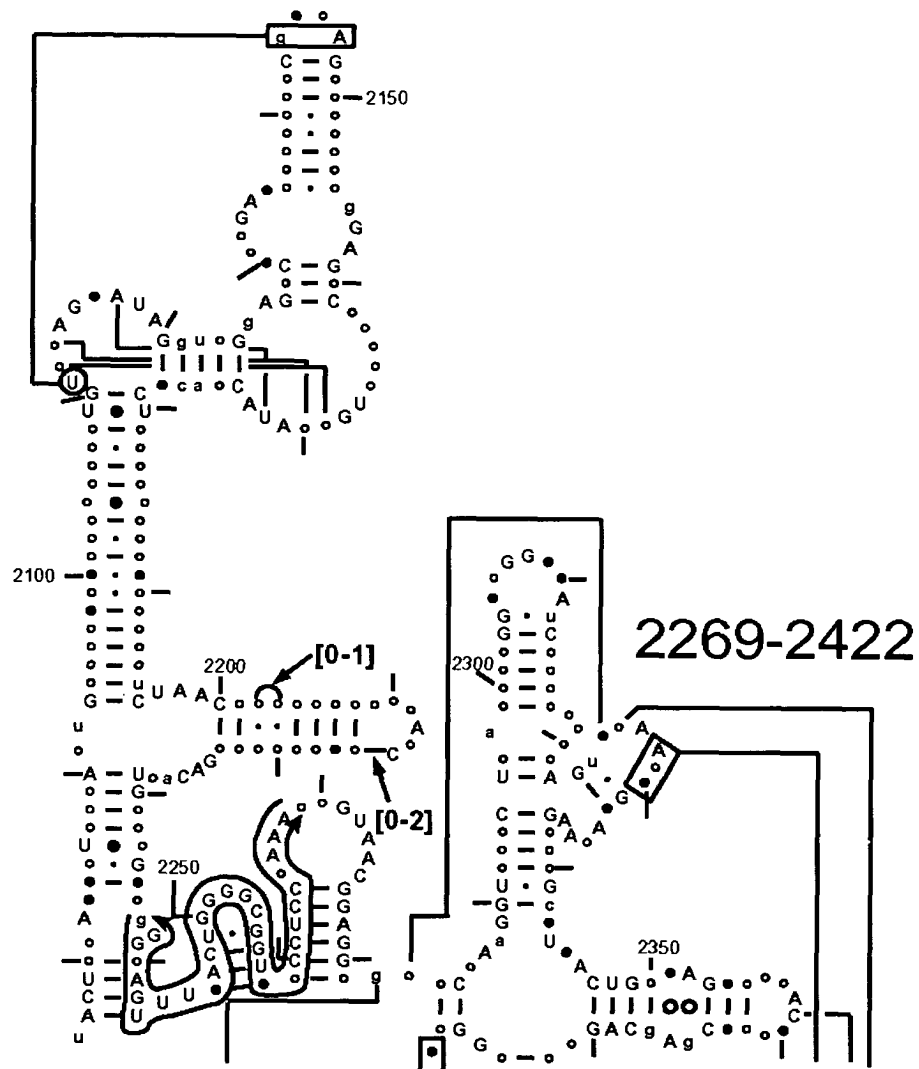
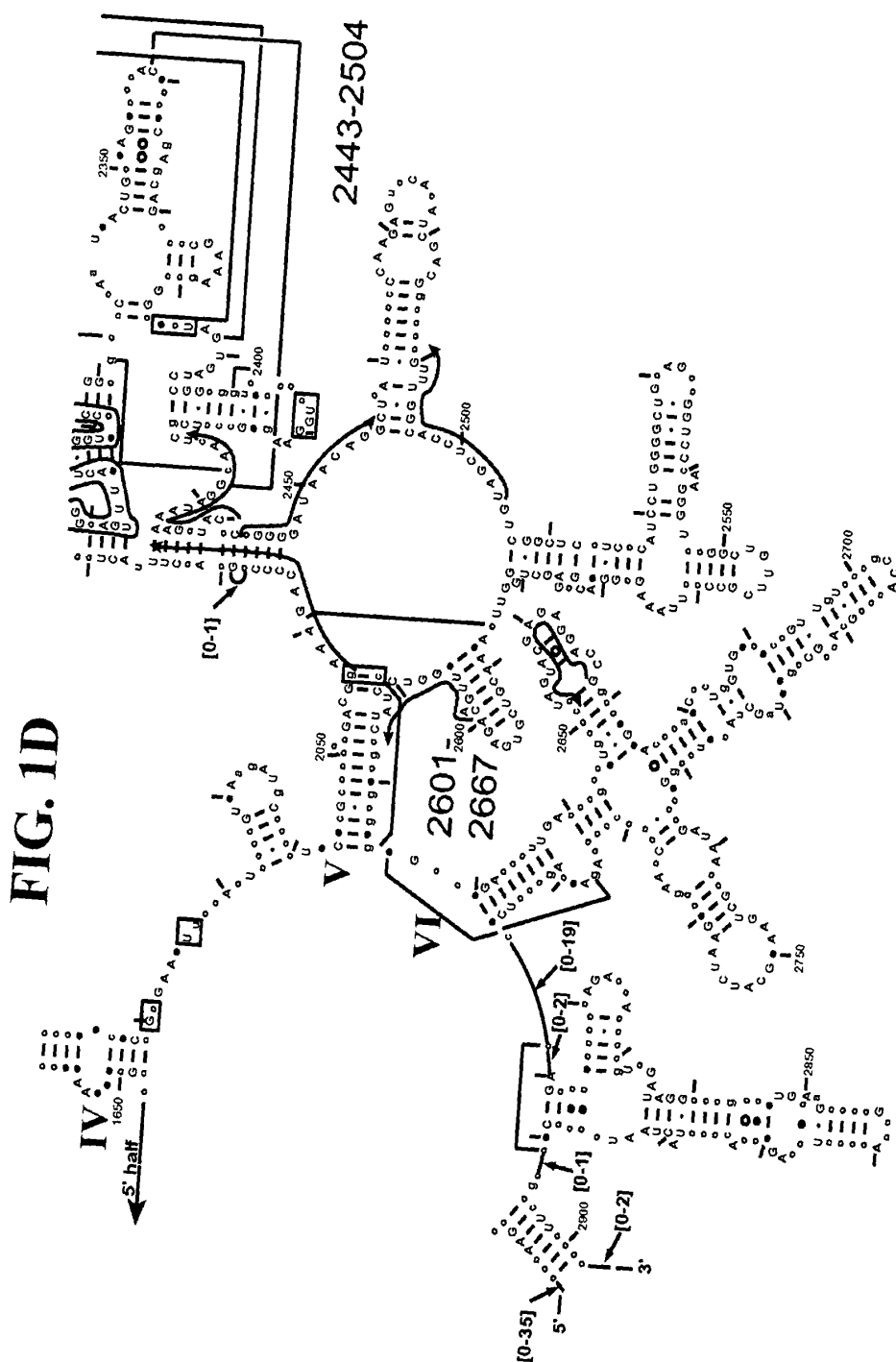


FIG. 1C



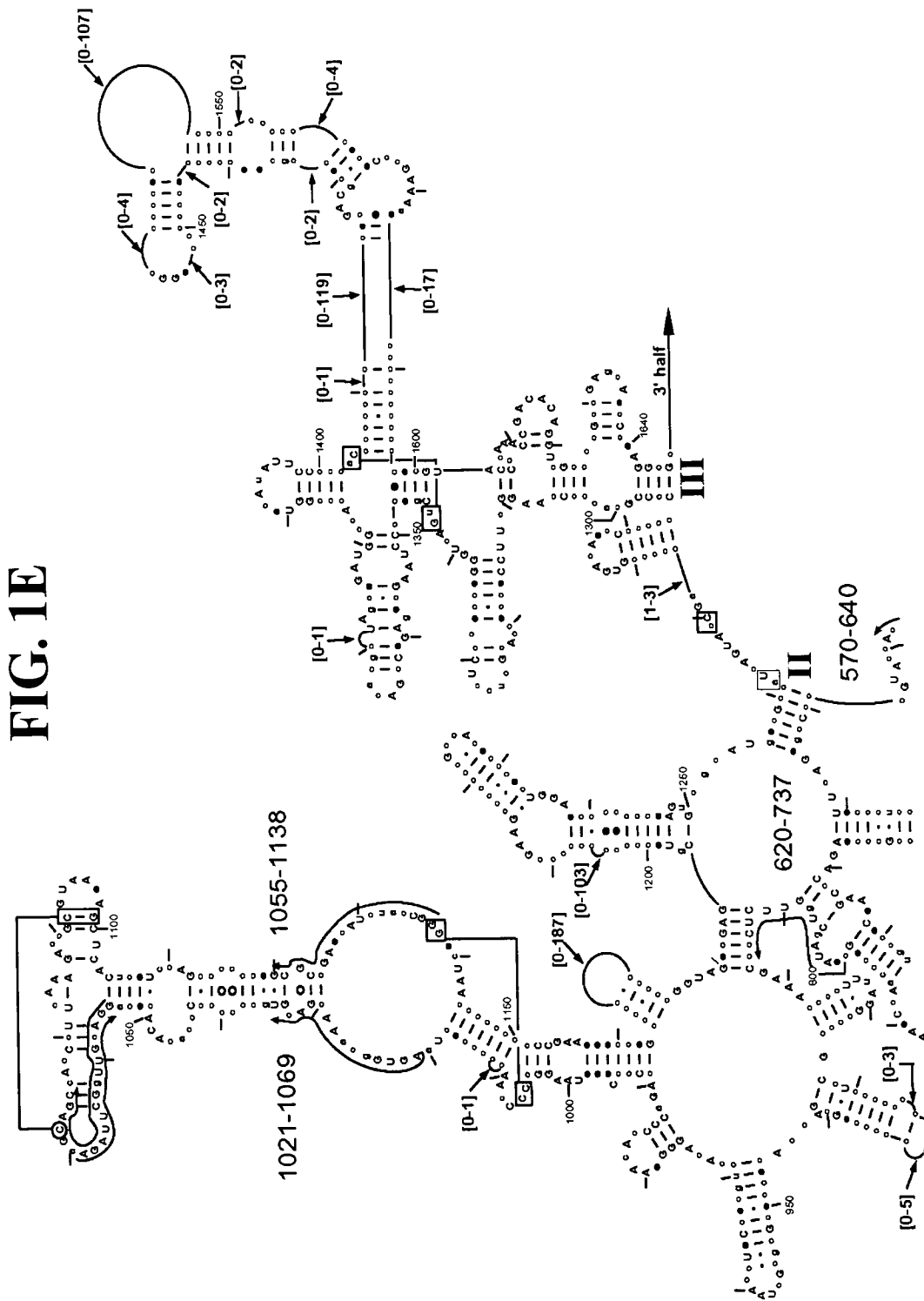


FIG. 1F

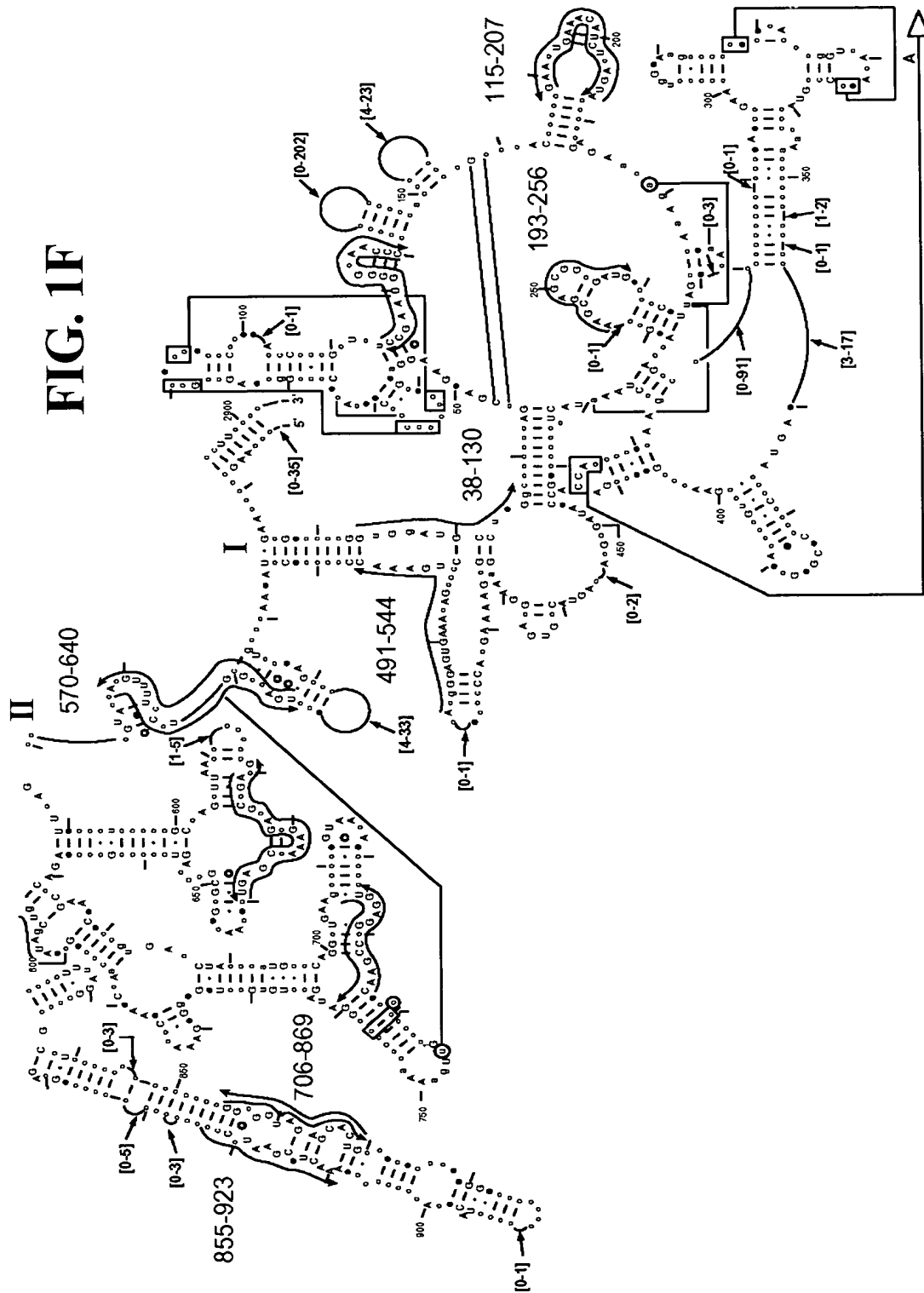


FIG. 1G

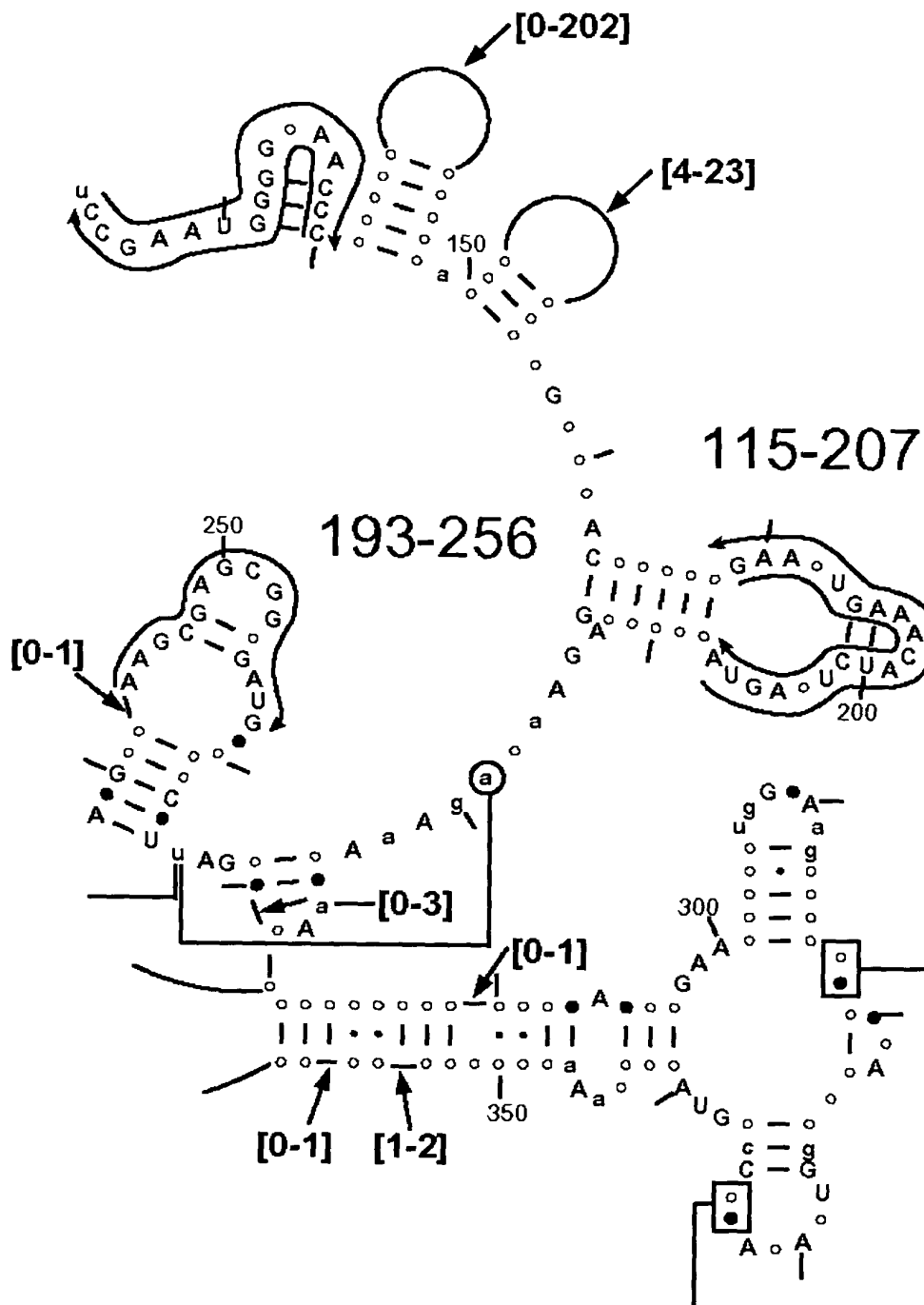


FIG. 1H

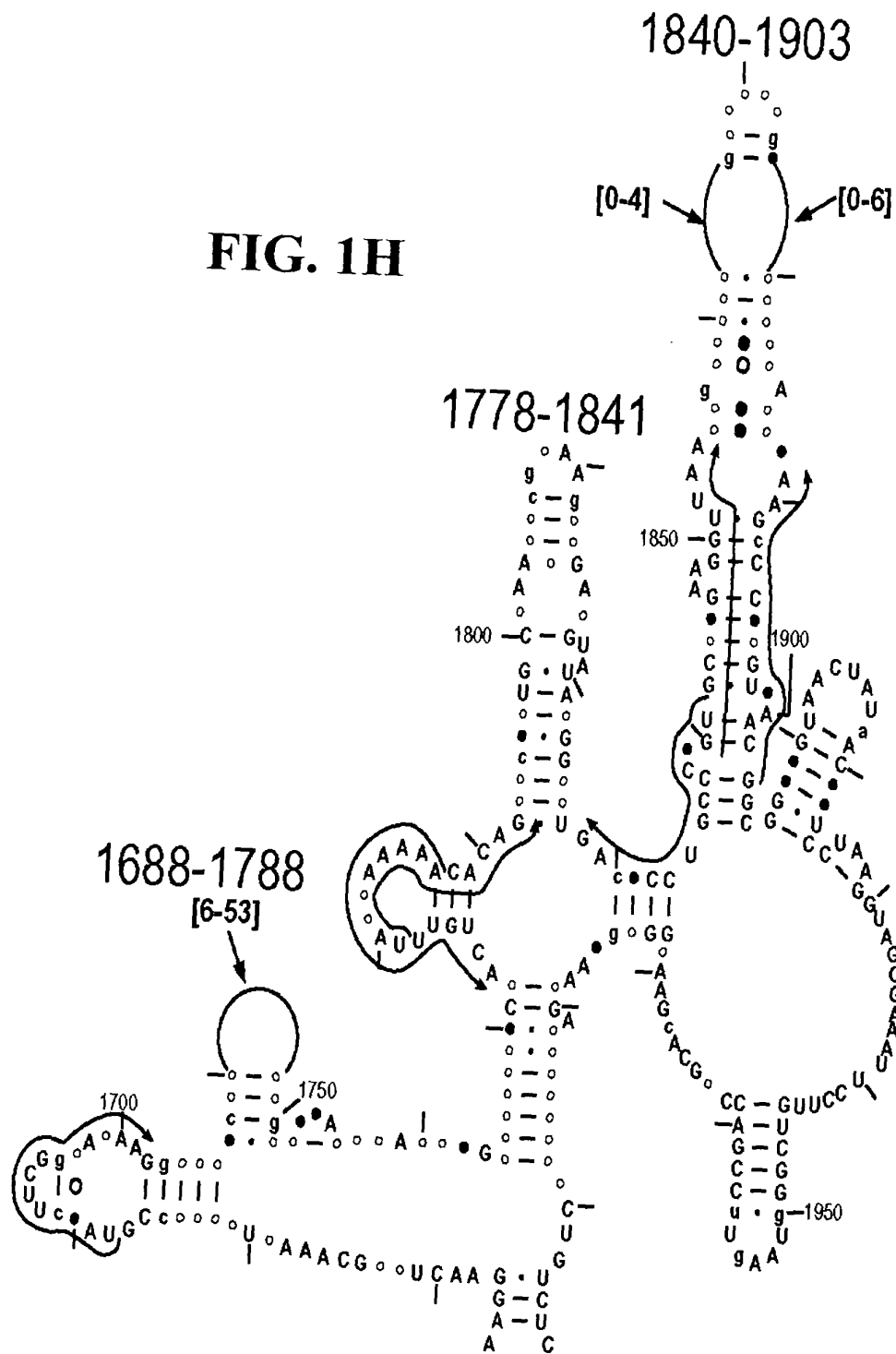


FIG. 2

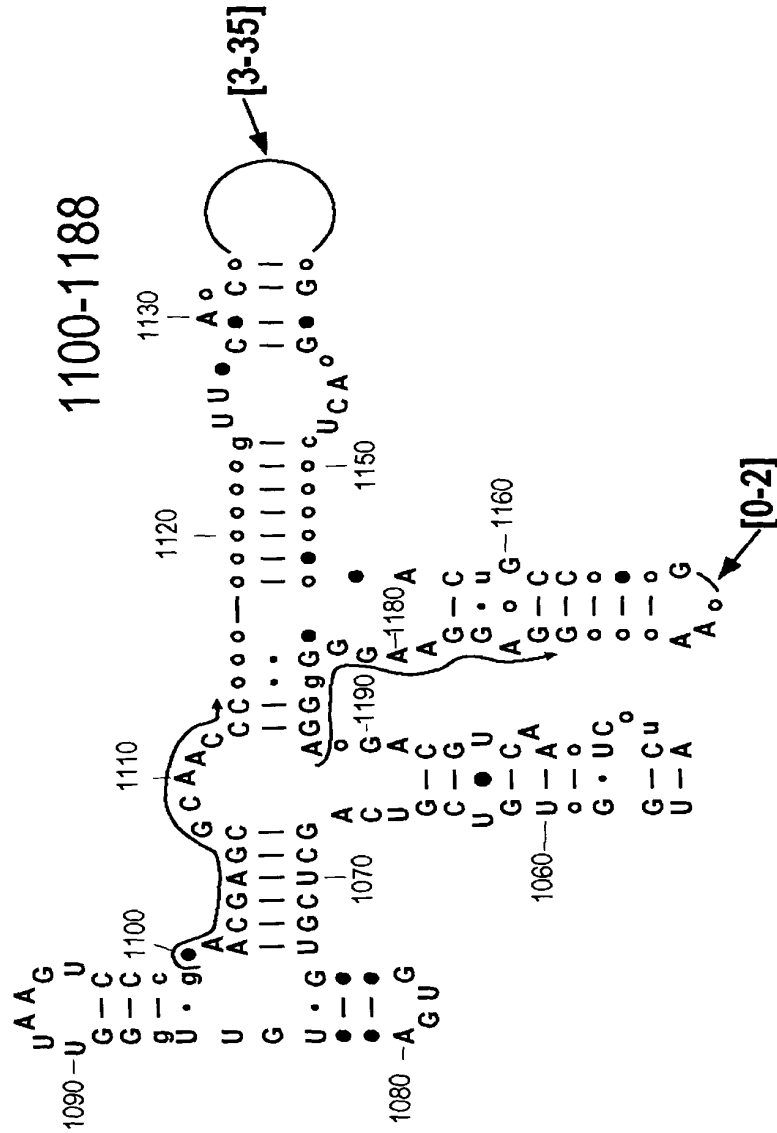


FIG. 3

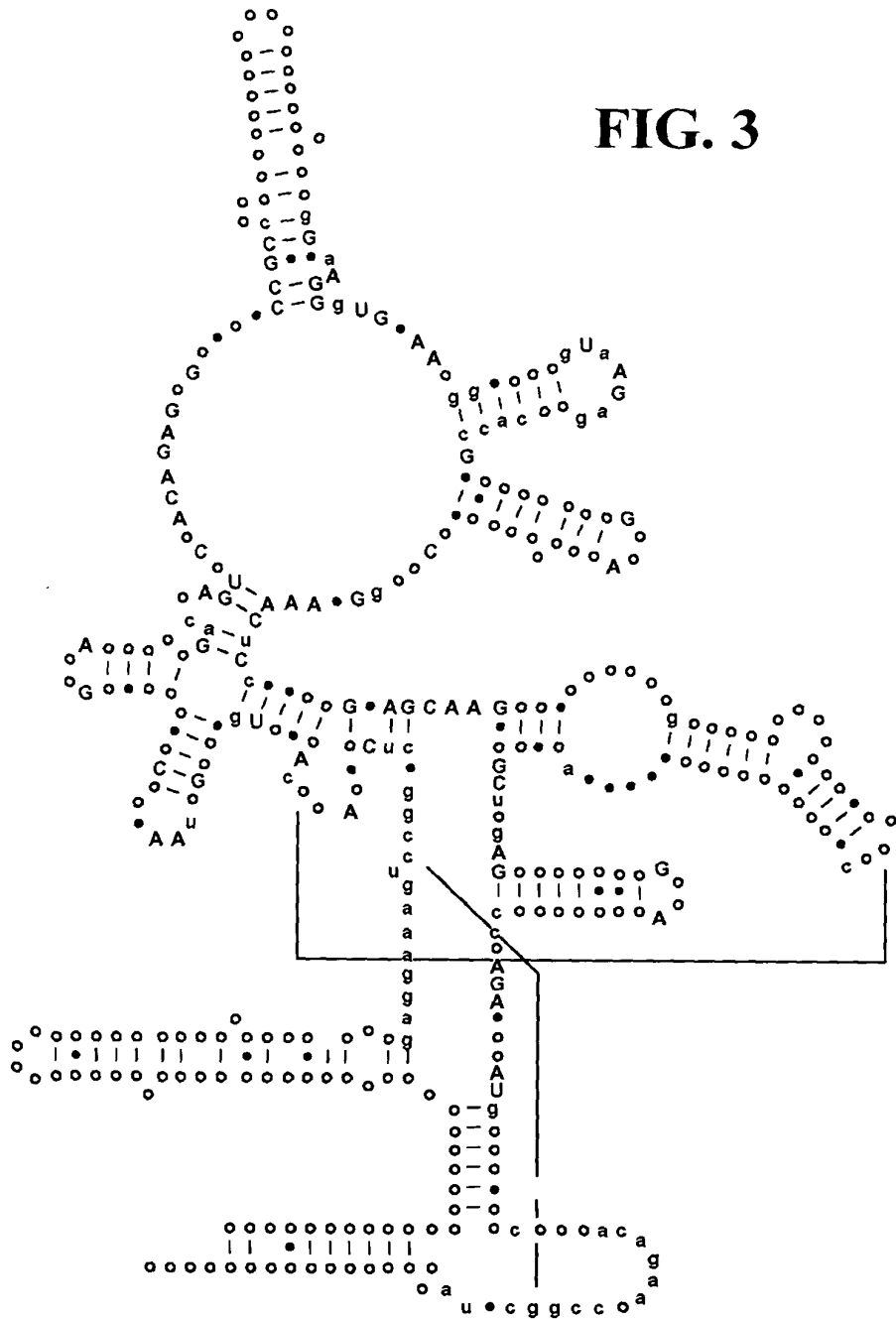


FIG. 4

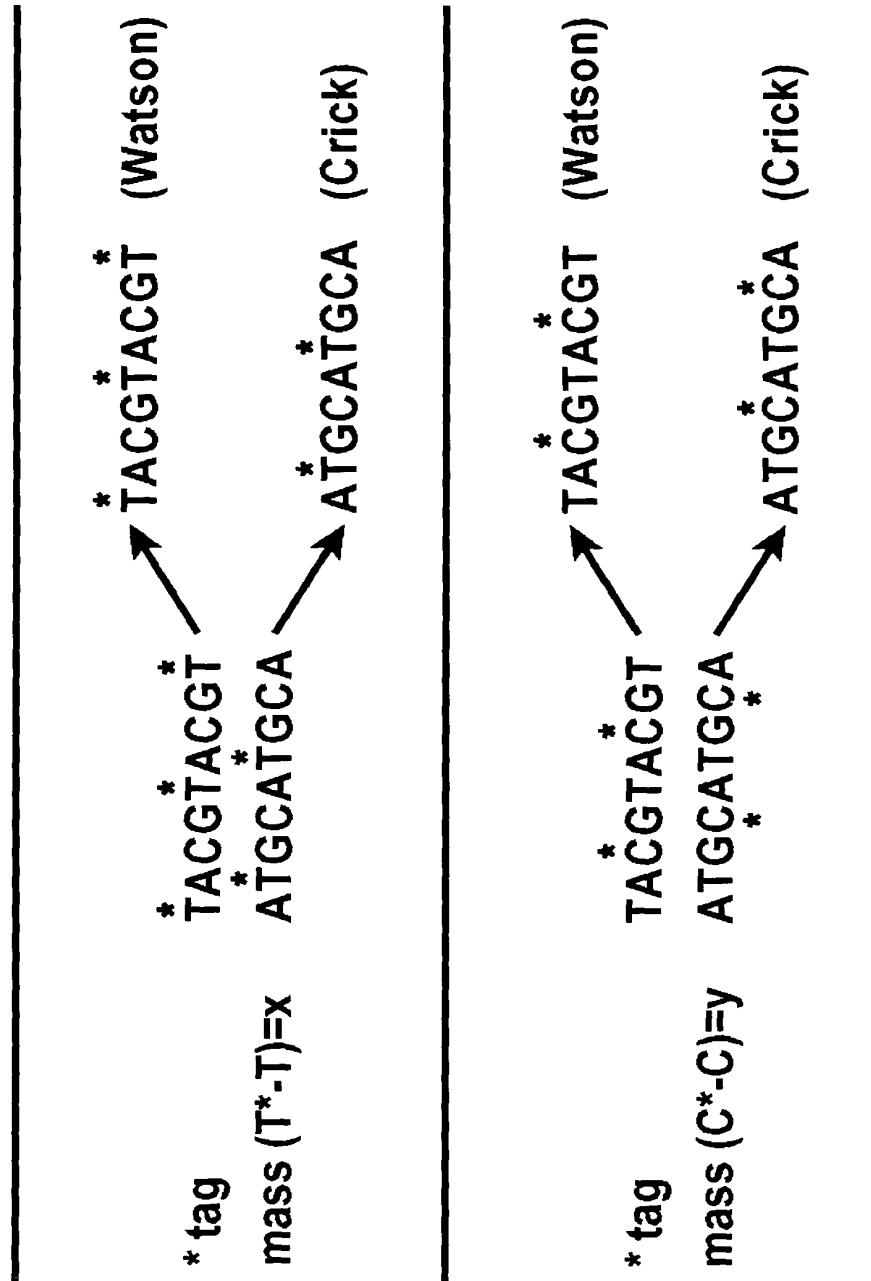
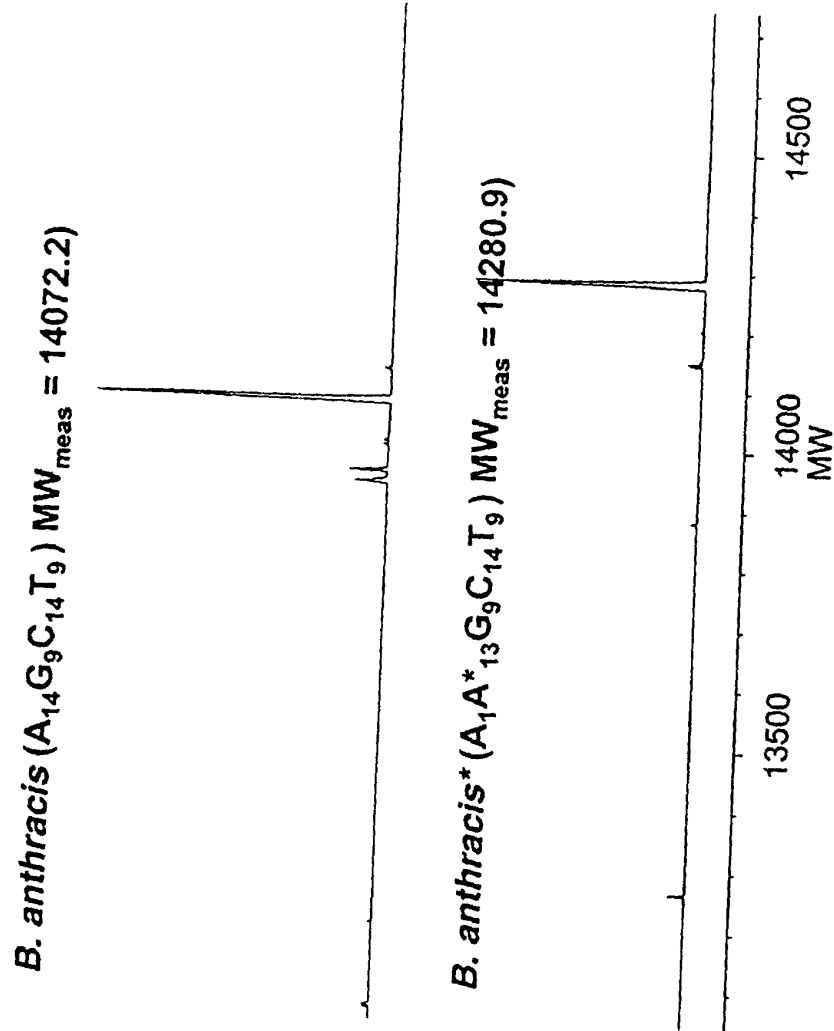


FIG. 5



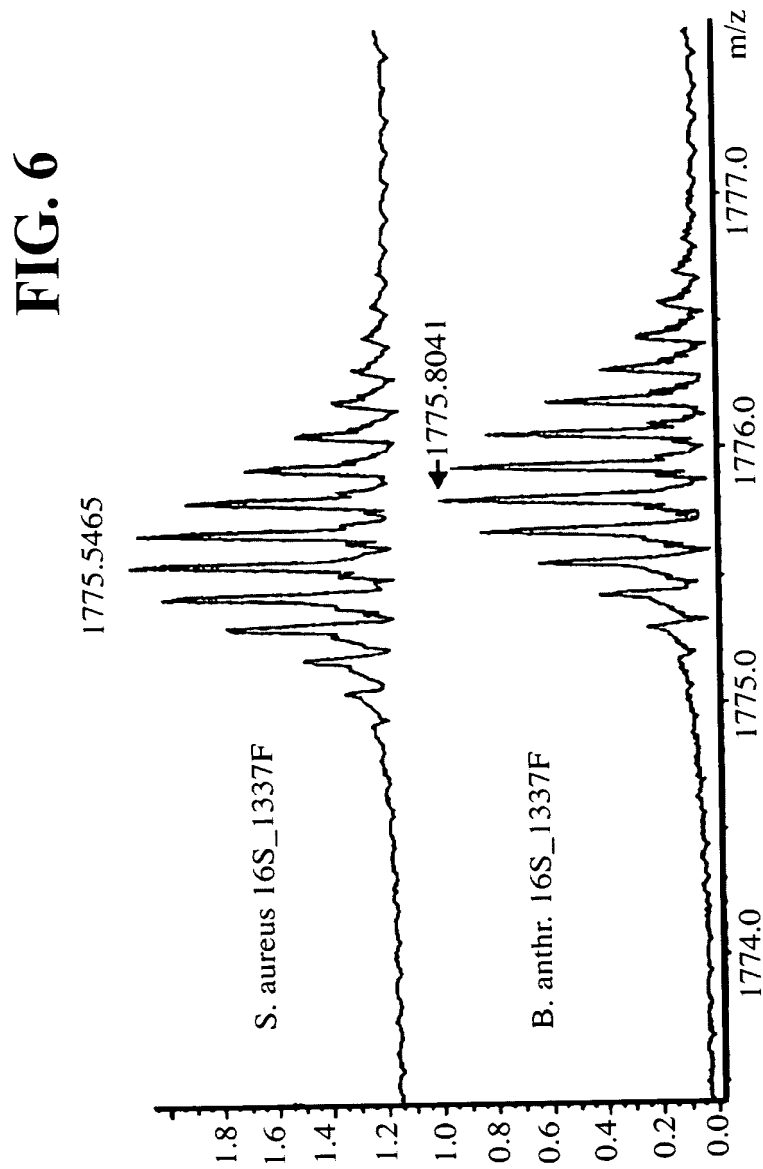


FIG. 7

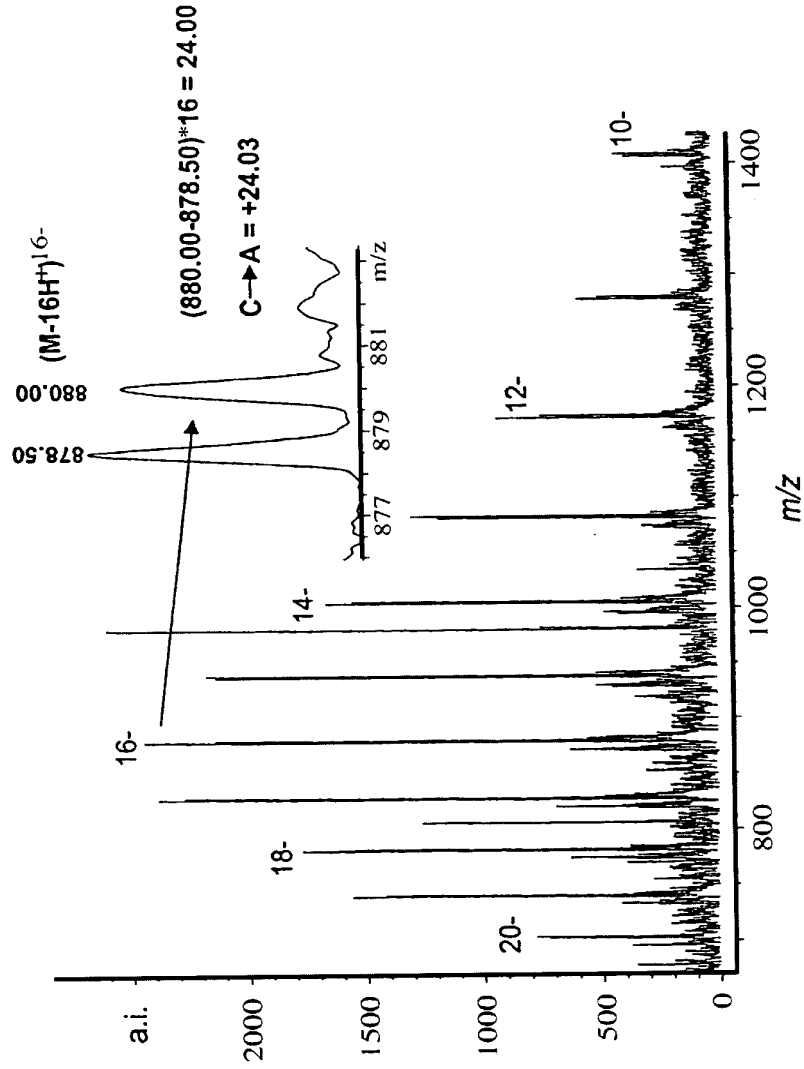
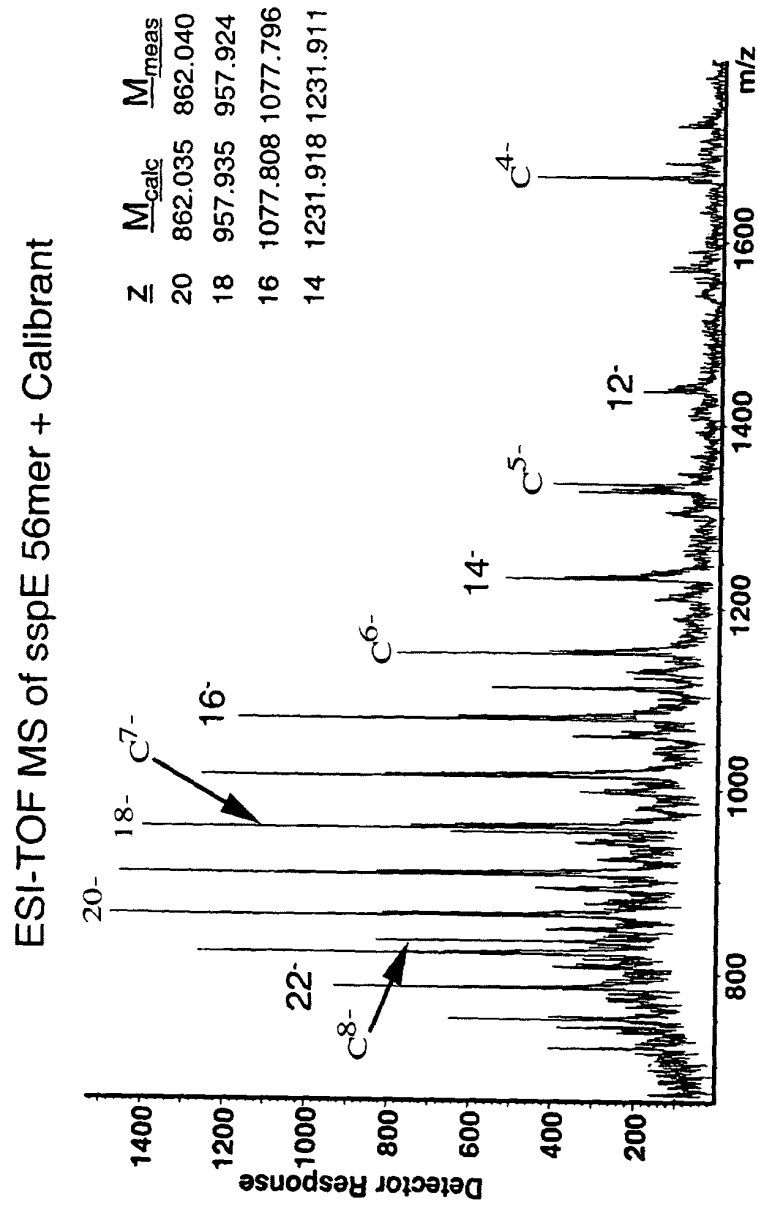


FIG. 8



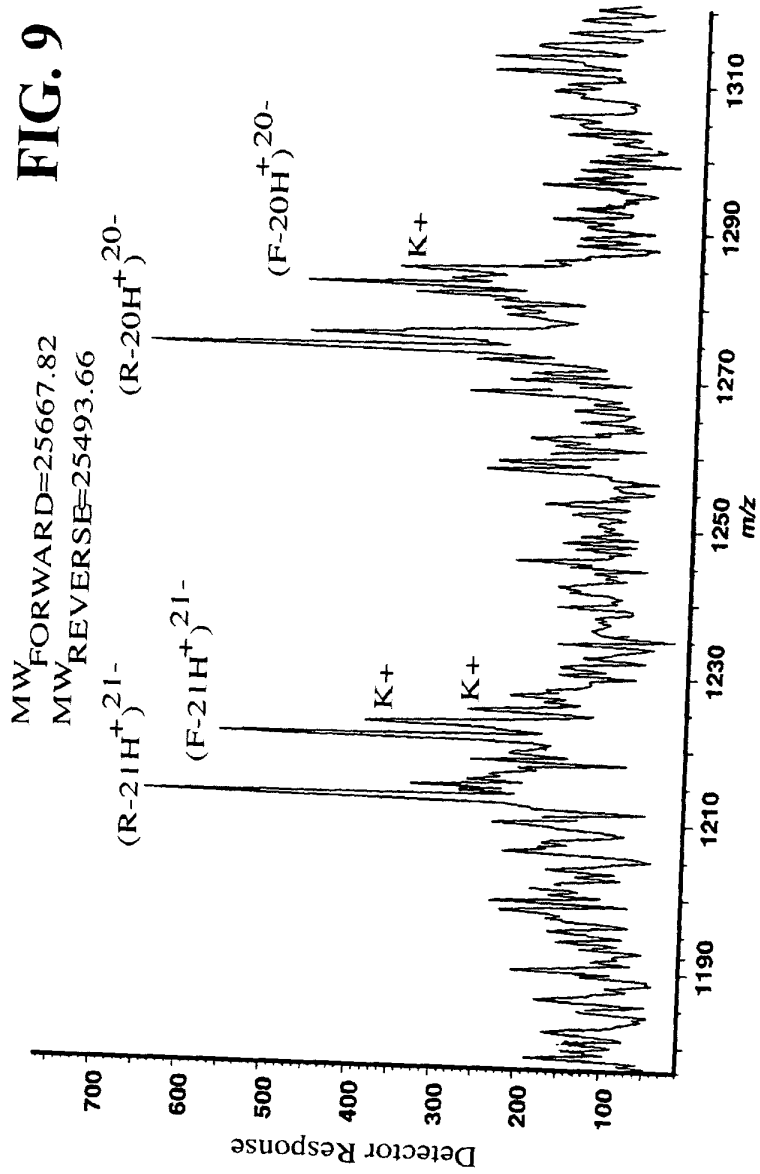


FIG. 10

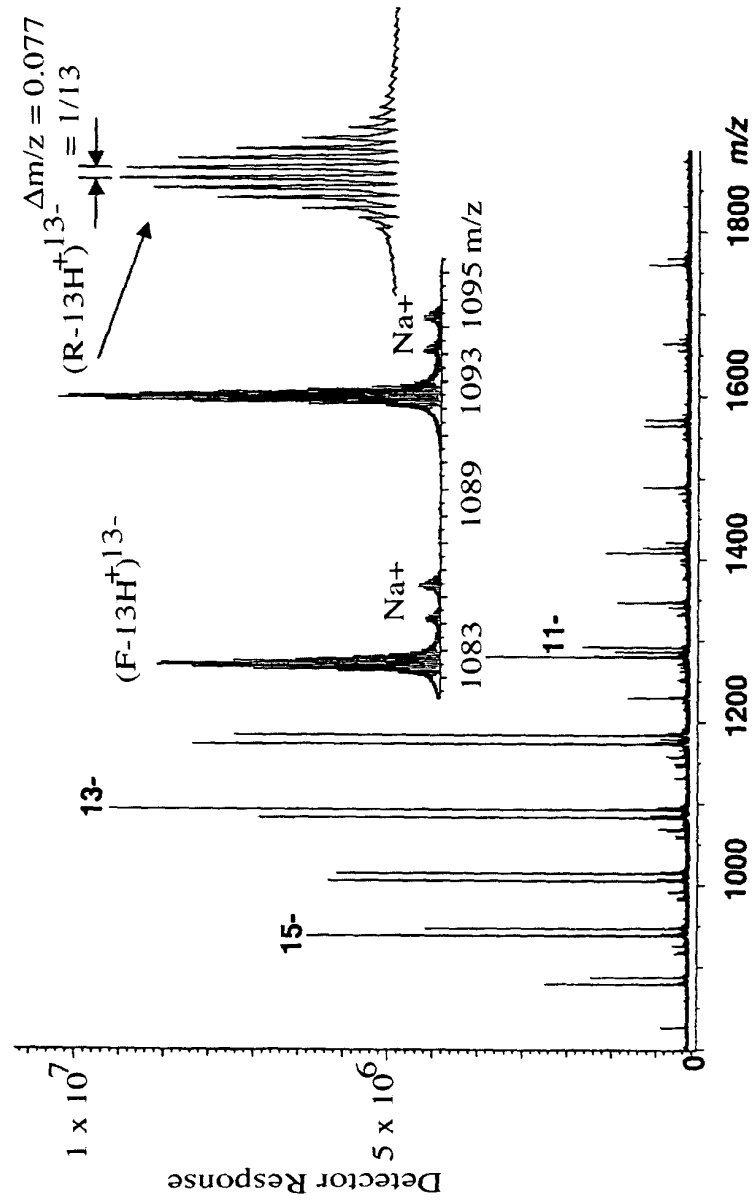


FIG. 11

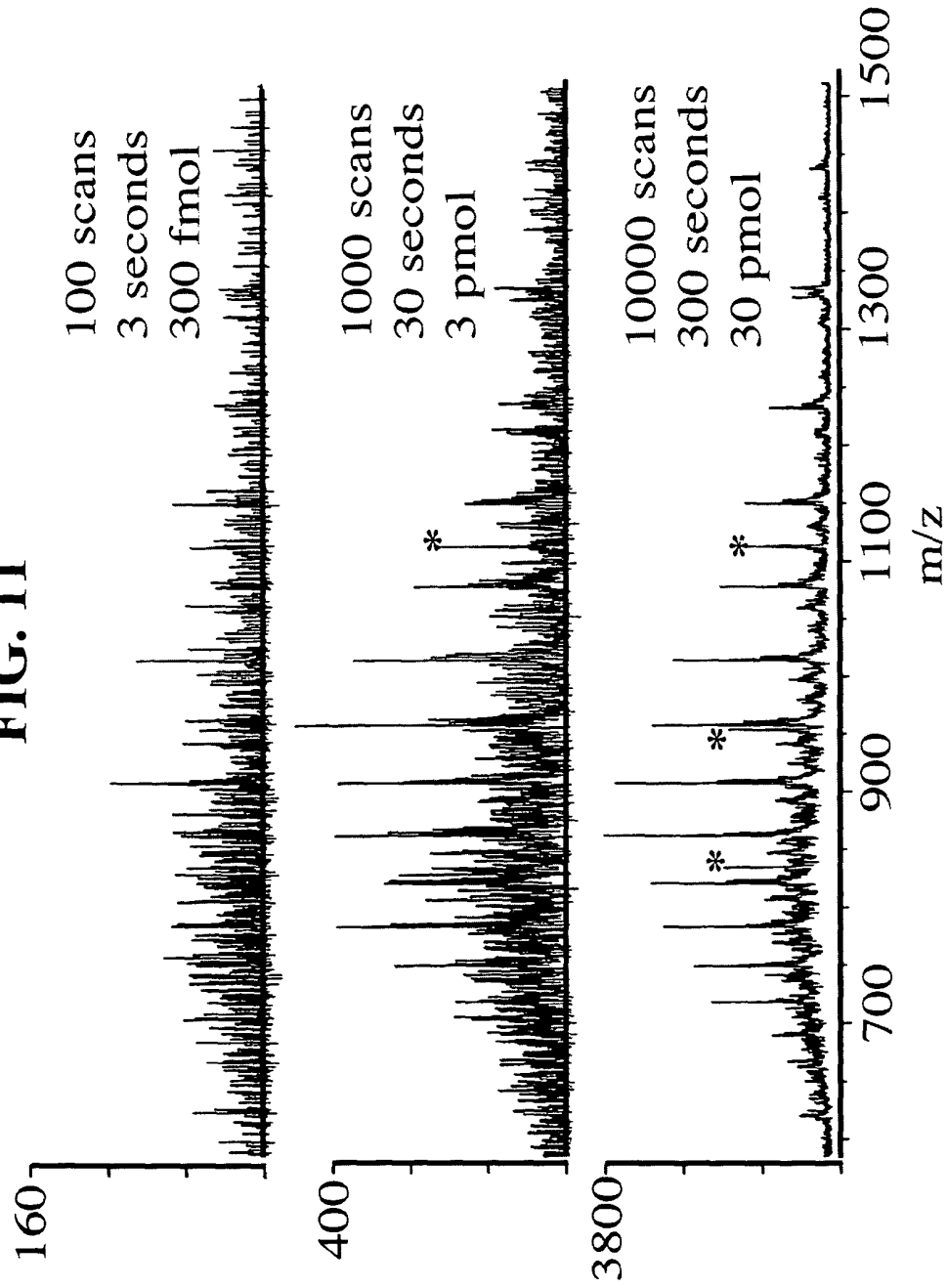


FIG. 12

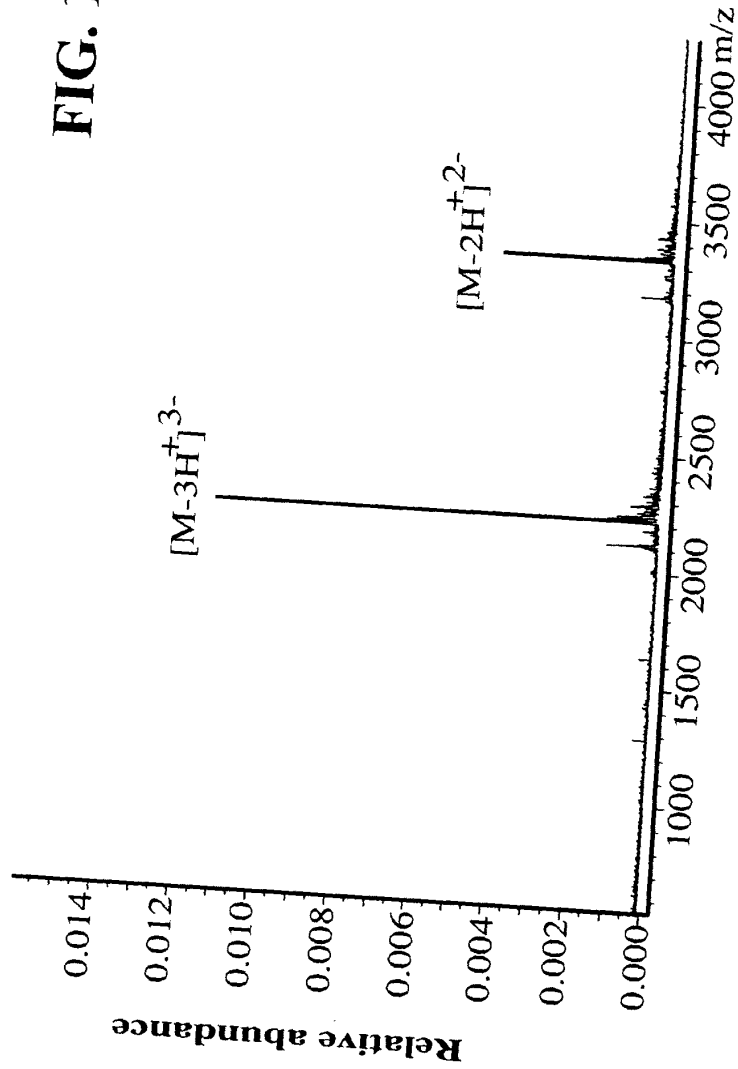


FIG. 13

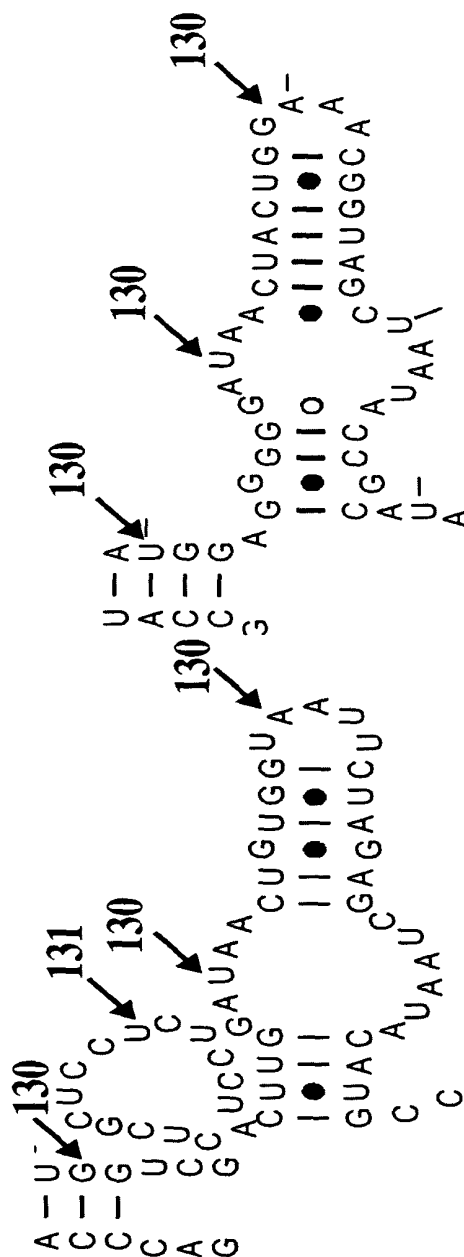
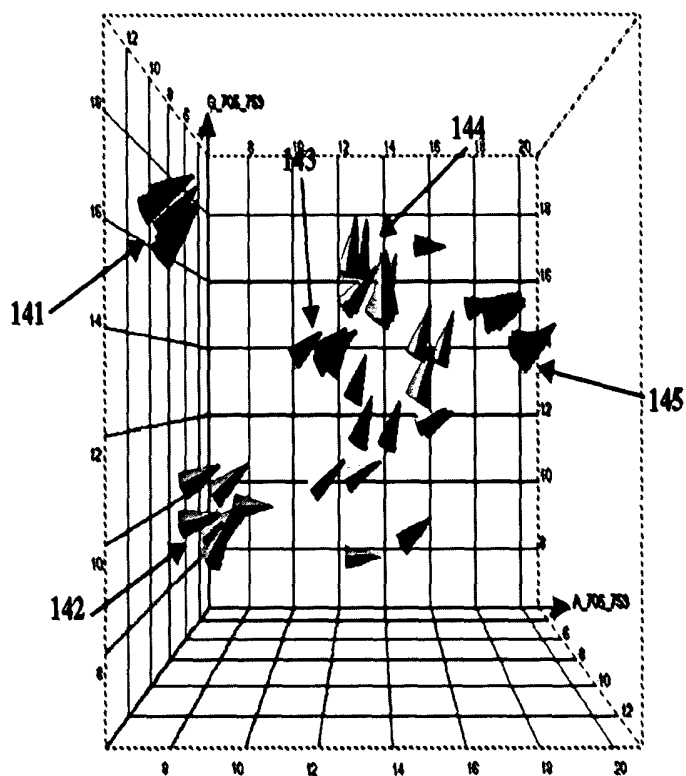


FIG. 14



Picornovirus RdRp 705-759

■ Encephalomyocarditis virus	□ Foot-and-mouth disease virus	▨ Polio	□ Rhinovirus
□ Enterovirus	■ Hepatitis A virus	■ Porcine enterovirus	▨ Simian Hepatitis A

FIG. 15

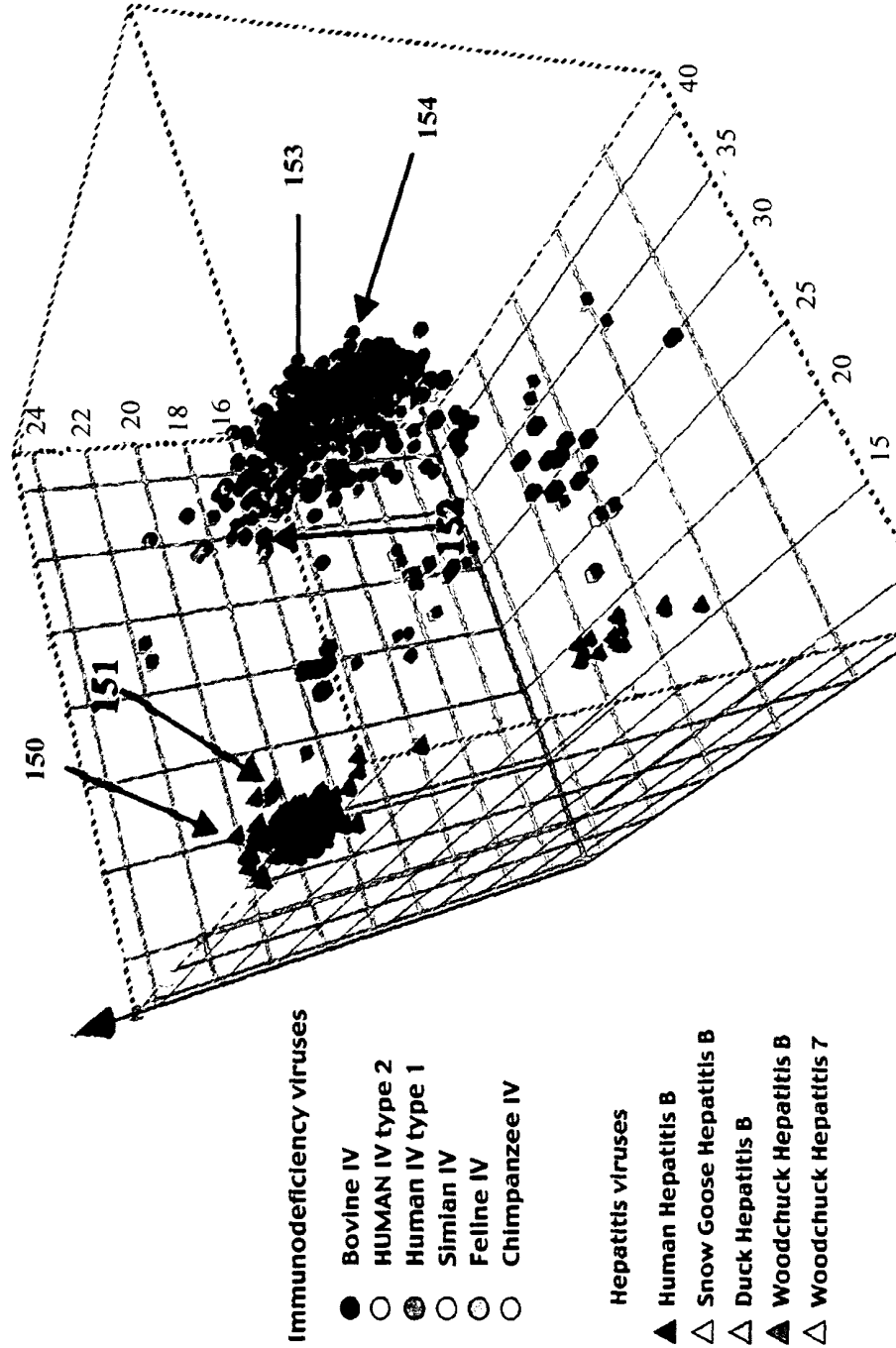
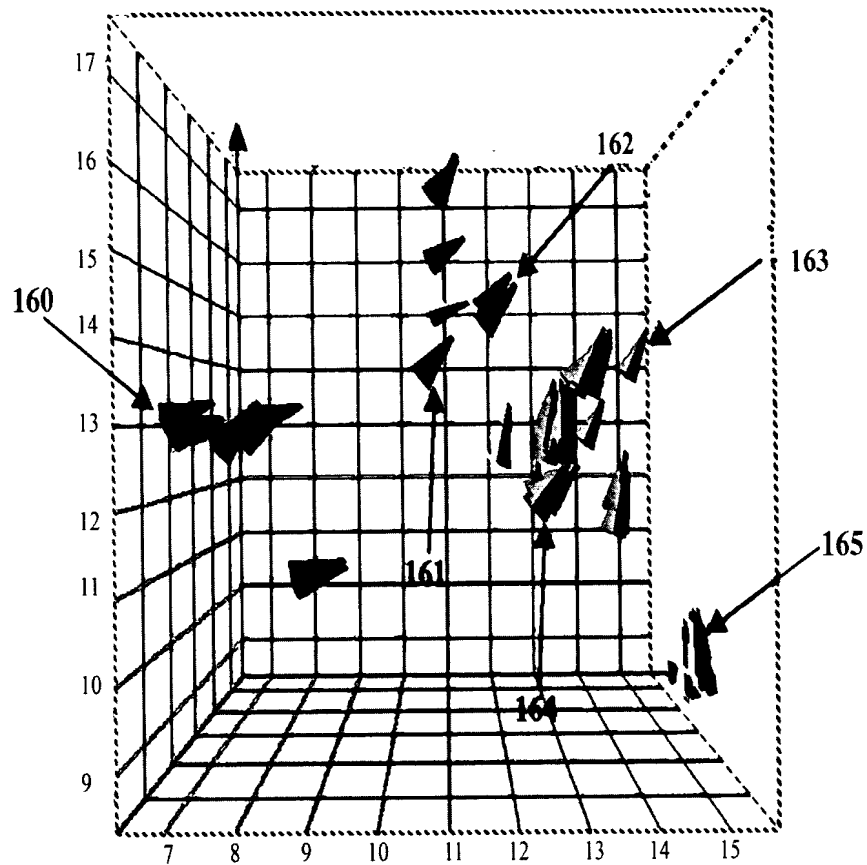


FIG. 16



- Flavi RdRp 2453-2493**
- | | | |
|-------------------|----------------------------------|-------------------------------|
| Dengue virus type | Japanese encephalitis virus | Tick-borne encephalitis virus |
| Dengue virus type | Kunjin virus | West Nile virus |
| Dengue virus type | Murray valley encephalitis virus | Yellow fever virus |

FIG. 17

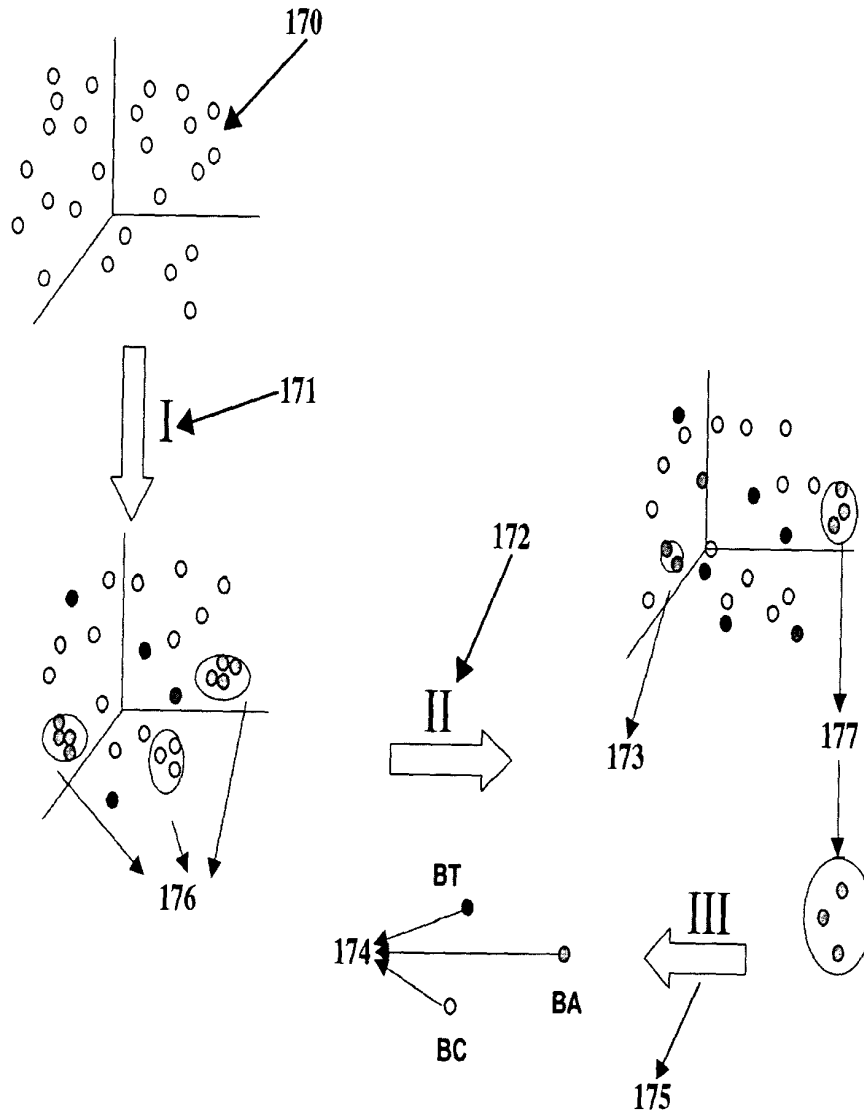
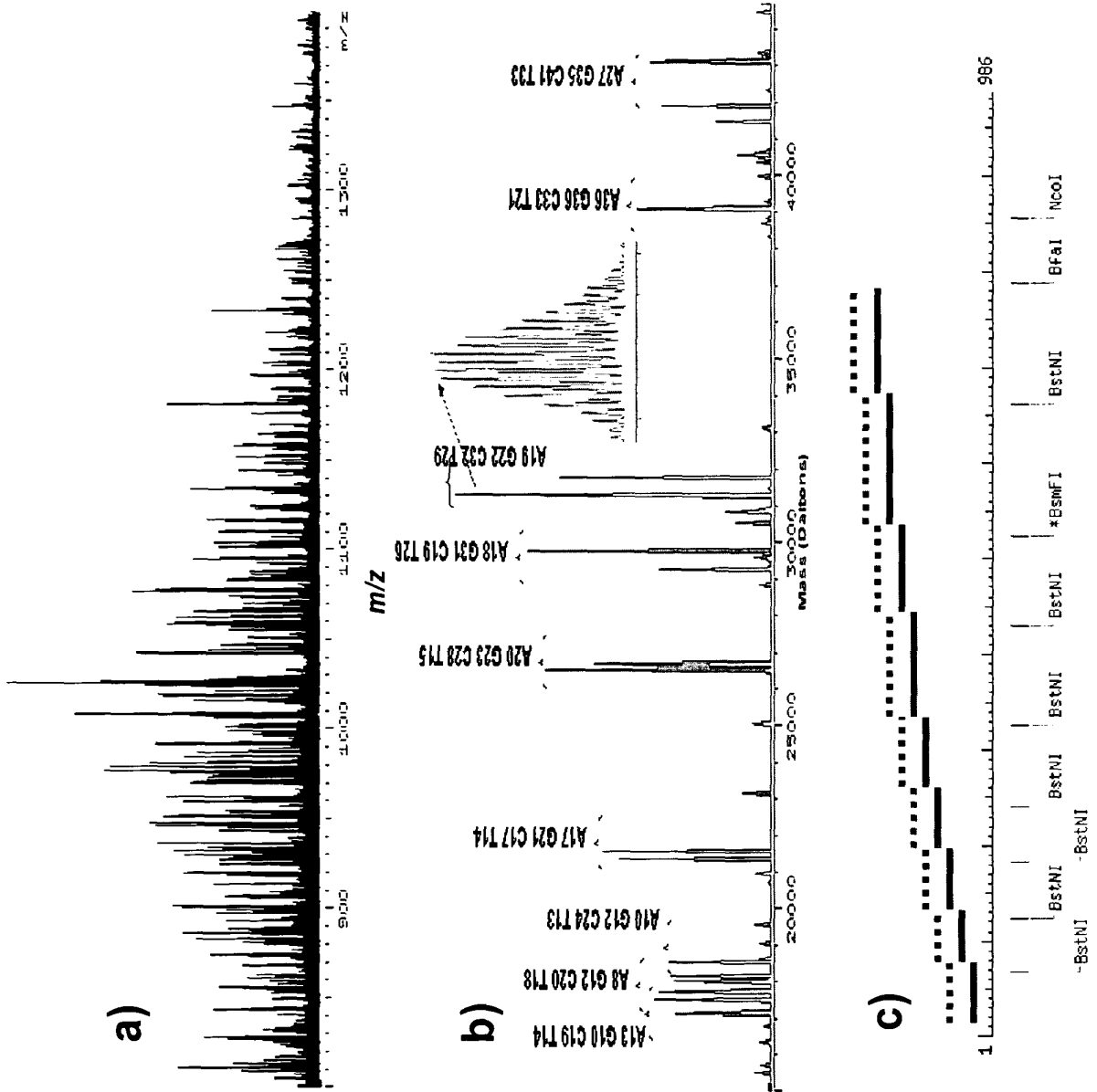


Figure 18



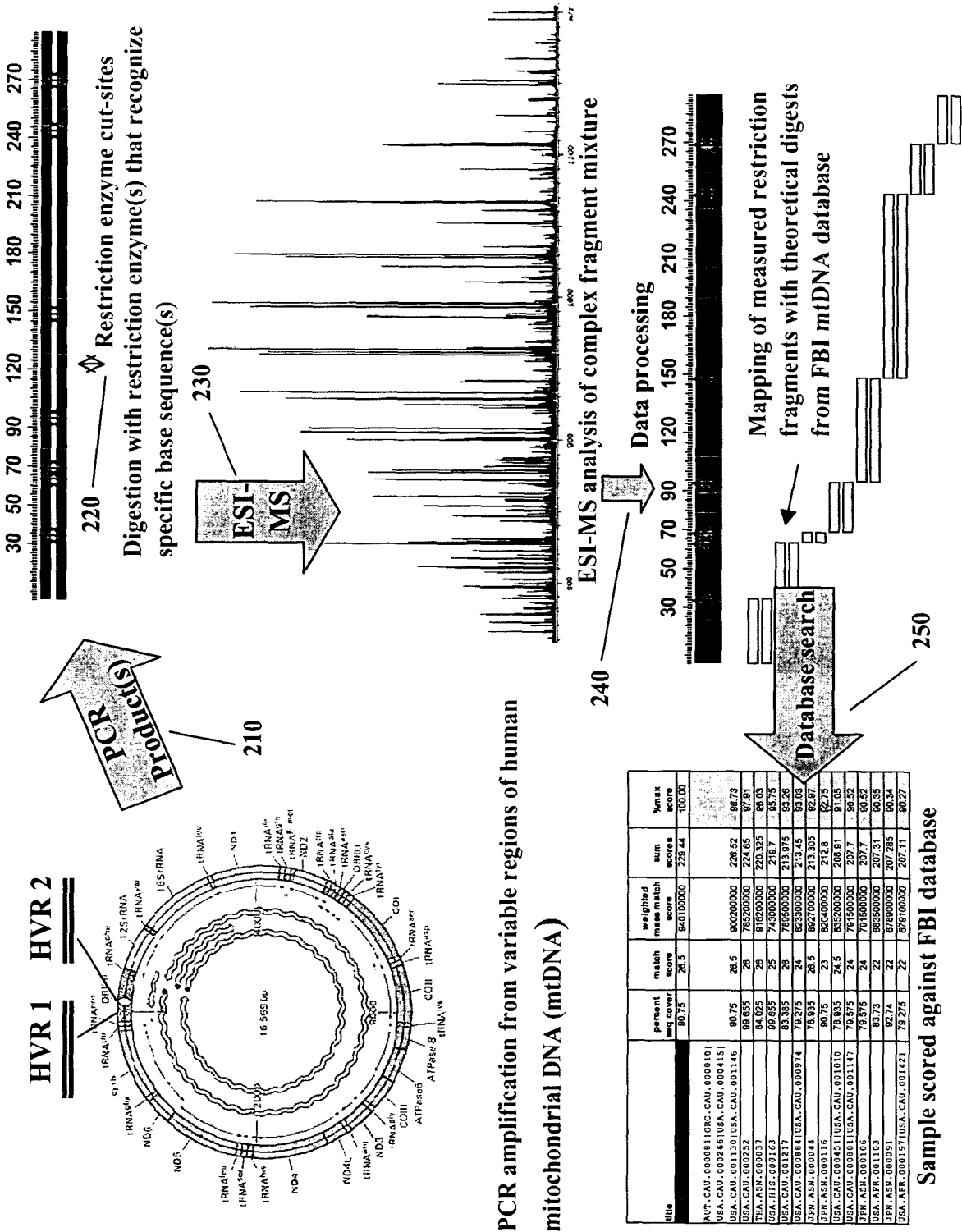
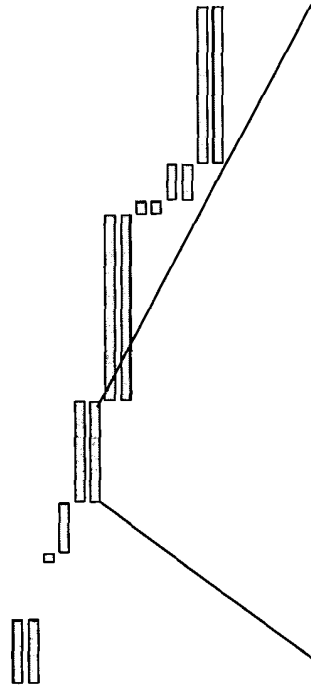


Figure 19

Sample 1: Heteroplasmy (mixture of lengths) is detrimental to sequencing approaches but does not adversely affect MS measurements

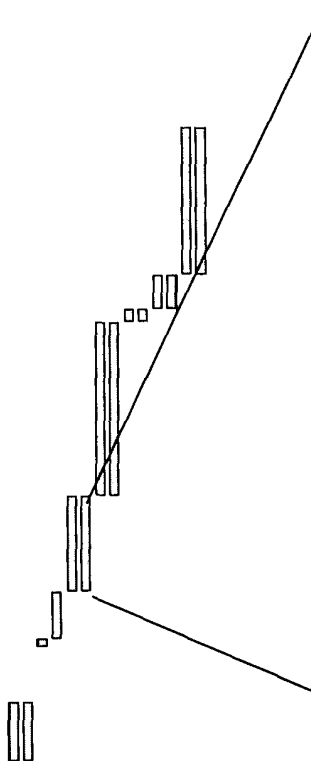
HV1-1-outer-variant1: p482_3_26_2003.pek, scan HV1-1-outer-variant2: p482_3_26_2003.pek, scan 1



Scan number: 1
Position: 94 to 145
Length: 52
Number of matched peaks: 1
Fragment seq: CAAATCAACATCAAAACCCCCCCCATGCTTACAAAGCAAGT
Average Predicted fragment mass: 15753.66266 ± 0.00000 daltons
Average matched peak mass: 15753.63000 ± 0.00000 daltons
Total peak abundance: 4.01E+06
Average peak abundance: 4.01E+06 ± 0.00E+00
Maximum peak abundance: 4.01E+06
Weighted average match error: 2.07327 ± 0.00000 ppm
Raw average match error: 2.07327 ± 0.00000 ppm
Weighted average peak fit: 0.05900 ± 0.00000
No ambiguous assignments in group

(opposite strand also observed)

HV1-1-outer-variant1
HV1-1-outer-variant2



Scan number: 1
Position: 94 to 146
Length: 53
Number of matched peaks: 1
Fragment seq: CAAATCAACATCAAAACCCCCCCCATGCTTACAAAGCAAGT
Average Predicted fragment mass: 16042.70903 ± 0.00000 daltons
Average matched peak mass: 16042.68880 ± 0.00000 daltons
Total peak abundance: 9.97E+06
Average peak abundance: 9.97E+06 ± 0.00E+00
Maximum peak abundance: 9.97E+06
Weighted average match error: 1.26121 ± 0.00000 ppm
Raw average match error: 1.26121 ± 0.00000 ppm
Weighted average peak fit: 0.02100 ± 0.00000
No ambiguous assignments in group

(opposite strand also observed)

acataaaaaaaccaatccacatcaaaacccccccccatgcttacaagcaagt
acataaaaaaaccaatccacatcaaaacccccccccatgcttacaagcaagt

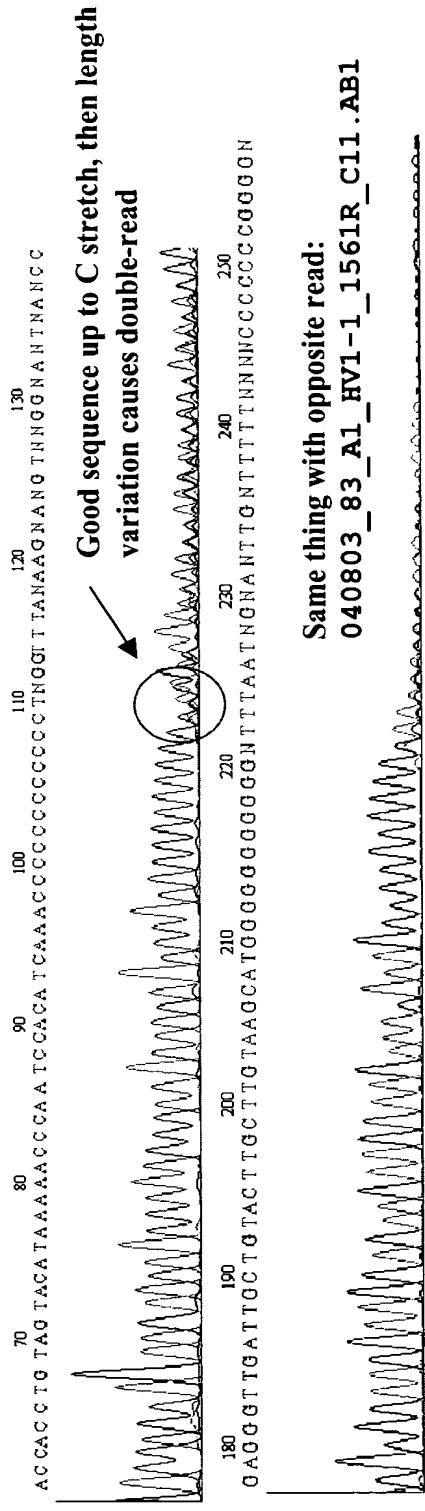
Heteroplasmic region

Figure 20A

Figure 20B

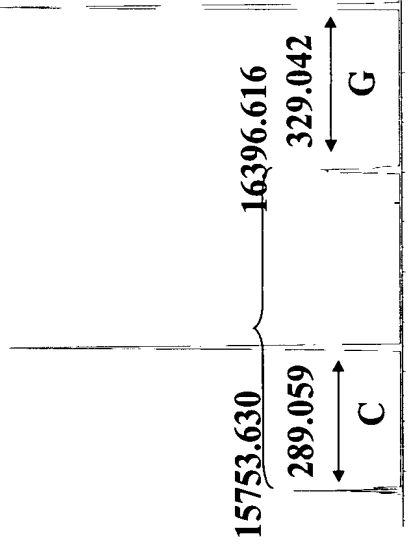
MS Approach Succeeds Where Conventional Sequencing Fails

Sequences differ in length by one base in the 'C' stretch. Both variants appear in digest data. Sequencing profile also points to a length variation in this region: Example trace: 040803_81_A1_HV1-1_1560F_A11.AB1



Same thing with opposite read:
040803_83_A1_HV1-1_1561R_C11.AB1

16042.689 16725.670



MS detects multiple species simultaneously while sequencing requires pure sample for maximum information content

Ratio of short to long alleles is 1:3